ORIGINAL ARTICLE

The contribution of single antigen measles, mumps and rubella vaccines to immunity to these infections in England and Wales

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Objective: To obtain information on the use of single antigen measles, mumps and rubella vaccines to improve estimates of population immunity and help predict outbreaks.
Design: We requested information from providers of single antigen vaccines and from the Medicine and Healthcare products Regulatory Agency on requests for importation of single antigen measles and mumps vaccines.
Setting: England and Wales.
Main outcome measures: Number of doses of single measles, mumps and rubella vaccine, by age of child (in months), year given and area of residence, and number of children who have received all three single vaccinations.
Results: Of 27 providers identified, 13 held single site clinics: nine were individual general practitioners and five held clinics at multiple sites. Data were received from 9/27 (33%) providers operating 40/74 (54%) clinic sites. We received information on 60 768 vaccinations administered by single vaccine providers and 269 917 doses requested for importation. For children born in 2001/2002, the minimum estimates for the proportion who received single measles vaccine are 1.7% in 2001 and 2.1% in 2002, with a reasonable maximum estimate of 5.6% over the 2 years. For single mumps vaccine, the minimum estimates are 0.3% in 2001 and 0.02% in 2002, with a maximum estimate of 4.0%.
Conclusion: The contribution of single vaccines to immunity is small in comparison to that of the combined measles, mumps and rubella vaccine (MMR). For recent birth cohorts this contribution could increase routine coverage for measles-containing vaccines by around 2%, still below the level of immunity required to sustain elimination.

After the introduction of a combined measles, mumps and rubella vaccine (MMR) in the United Kingdom (UK) in October 1988, uptake of the first dose of vaccine amongst 2-year-olds in England reached a peak of 92% in 1995. Following speculation that the vaccine might be linked with Crohn's disease, and then subsequently with autism, MMR uptake began to decline. Despite a series of subsequent reviews demonstrating the safety of MMR,[1] coverage in 2004 was 81%.[2] There have been concerns that outbreaks of measles are increasingly likely to occur due to low uptake of the MMR vaccine and accumulating numbers of unprotected children in the UK.[3]

Levels of population protection against each of the three infections may, however, be higher than those estimated by MMR coverage. While some children have not received any vaccination against these infections, a number of parents have chosen to vaccinate their children with single antigen measles, mumps or rubella vaccines.

We aimed to obtain information on the use of single antigen vaccines in England and Wales to improve the estimate of population immunity to measles, mumps and rubella that could inform predictions of outbreaks.

METHODS

Identification of providers of single antigen vaccines was done through a ''snowballing'' process, through email discussion groups (eg, ''vaccimmuk'' and ''CCDC-UK'') and websites (eg, www.jabs.org.uk). Information requested from each provider was similar to that reported in the routine COVER (Coverage of Vaccination Evaluated Rapidly) programme (http://www.hpa.org.uk/infections/topics_az/vaccination/vac_cover.htm). It included (1) details of clinics (sites and frequency); (2) number of doses of each of the three single antigens (measles, mumps and rubella) administered, by age of child (in months), year given and geographical area of residence; and (3) number of children who have received all three single vaccinations, by age, year and area.

Despite concerted effort and long delays, however, data were only received from nine of 27 providers (see below). We therefore determined a minimum and maximum estimate of vaccine coverage as follows.

For the minimum estimates, the pattern of vaccine use for each antigen administered by year of birth was assumed to be the same for the three providers who reported date of birth and for the other six providers who forwarded less detailed information. We assumed that this pattern was stable in each year and that the providers operated during the whole period. Data from these nine providers were then used to estimate the minimum number of doses of single antigen vaccines administered by birth cohort and the proportion of all children born in each year in England and Wales who received each vaccine. This excluded those providers who did not provide data.

For the maximum estimates, data were obtained from the Medicine and Healthcare products Regulatory Agency (MHRA) on the number of requests for importation of single antigen measles and mumps vaccines. Data were not available for rubella vaccine as a licensed supply was available in the UK

Abbreviations: COVER, Coverage of Vaccination Evaluated Rapidly; MHRA, Medicine and Healthcare products Regulatory Agency; MMR, measles mumps and rubella vaccine; UK, United Kingdom

Figure 1 Geographical distribution of 74 clinics providing single antigen measles, mumps and rubella vaccination in England and Wales.

until fairly recently, so maximum figures could not be calculated for this antigen.[4] To estimate the maximum number of doses that could have been administered, we assumed that all vaccine requested for importation was administered and vaccine was only given as a first dose. After approval, some vaccines may not be imported, and it is thought that the actual number of doses imported may be 20–30% of the number notified (Andrew McKendrick, MHRA, personal communication). Furthermore, even when imported, it is not certain if (and when) vaccination has been administered. We therefore repeated our calculations with a more cautious assumption that only 30% of doses requested were administered.

RESULTS

We identified 27 providers, who fall into three broad groups: multiple site providers (n = 5), single site clinics (n = 13) and individual general practitioners (GPs; n = 9). Clinics operate from 74 sites and cover all regions of the country but are more prevalent in the south east of England (fig 1).

None of the 27 providers was able to provide the information in the format requested. Table 1 shows the numbers of vaccinations given by the nine providers (including four of the five multiple-site providers) who forwarded information. These represent 40/74 (54%) of all clinics identified, but the data provided covered different time periods. Between 1981 and September 2004 these 40 clinics administered at least 60 768 vaccinations.

The number of doses of single measles vaccine by birth cohort and the proportion of all children born in each year in England and Wales who received single antigen vaccines is shown in table 2. Of children born between 1992 and 2000, single antigen measles, mumps or rubella vaccines administered were sufficient to cover an average of 0.09%, 0.08% and 0.07%, respectively. For measles vaccine, the proportion covered increased with each successive birth cohort to 2002. For mumps and rubella vaccine, there was a decline in the more recent cohorts (table 2).

The MHRA provided data for the 17-month period April 2002–August 2003. During this period, there were 5101 applications to import single measles vaccine and 3041 applications for single mumps vaccine. For single measles vaccine, 156 157 doses were requested for importation in this

Table 1 Number of single antigen measles, mumps and rubella vaccines administered by providers who forwarded data*

	1999	2000	2001	2002	2003	2004	Total
Single measles							
Multiple site 1				256	814	85	1155
Multiple site 2		|----------14 092----------|					14 092
Multiple site 3			|----------2567----------|				2567
Multiple site 4				2118	805		2923
Single site 1			|----------4000----------|				4000
Single site 2			20	|----------412----------|			432
GP 1†				400	400		800
GP 2	|----------742----------|						742
GP 3†‡		150	254	2372	1318		4094
Total measles							30 805
Single mumps							
Multiple site 1					135		135
Multiple site 2		|----------3175----------|					3175
Multiple site 3			|----------320----------|				320
Multiple site 4				696	729		1425
Single site 1			|----------350----------|				350
Single site 2				|----------114----------|			114
GP 2	|----------360----------|						360
Total mumps							5879
Single rubella							
Multiple site 1				28	747	90	865
Multiple site 2		|----------14 533----------|					14 533
Multiple site 3			|----------778----------|				778
Multiple site 4				2256	805		3061
Single site 1			|----------4000----------|				4000
Single site 2				|----------112----------|			112
GP 2	|----------735----------|						735
Total rubella							24 084

*Figures with broken lines spanning several cells refer to the total doses given over the time period indicated.
†Children received at least one vaccination of which measles was usually the first; data on mumps and rubella unavailable. This GP's data started in 1981.
‡For this provider, these are the number of children, not number of vaccines given. As each child would probably have received more than one vaccine, this is a minimum estimate.
GP, general practitioner.

period. If these doses were only administered to children in the 2001/2002 birth cohorts (n = 1 190 756), and adjusting the figures (by dividing by 17 and multiplying by 24) to extrapolate to 24 months, this would give a maximum estimate of 18.5% of the birth cohort covered. Reducing the number of doses imported and given to only 30% of those notified, gives an estimate of 5.6%. For single mumps vaccine over this time period, the maximum number of doses that were imported was 113 760. Using the same assumptions, this gives an estimate of 13.5% covered if all vaccines were administered and 4.0% if only 30% of notifications resulted in vaccination.

DISCUSSION

Our results speculate on the potential contribution of single measles, mumps and rubella vaccines to immunity in children. The estimated numbers of doses are small in comparison with the number of doses of MMR administered, and for children born recently could increase routine coverage by a minimum of

Table 2 Estimates of the number of doses of single antigen measles, mumps and rubella vaccines in England and Wales by birth cohort*

		Measles		Mumps		Rubella	
Year of birth	Births	Estimated number of doses	% Birth cohort	Estimated number of doses	% Birth cohort	Estimated number of doses	% Birth cohort
Prior to 1992		54		14		30	
1992	689 656	12	0.002	5	0.001	8	0.001
1993	671 224	14	0.002	15	0.002	5	0.001
1994	664 256	24	0.004	31	0.005	17	0.003
1995	648 001	40	0.006	53	0.008	28	0.004
1996	649 489	91	0.014	177	0.027	108	0.017
1997	643 095	292	0.045	418	0.065	242	0.038
1998	635 901	663	0.104	658	0.104	606	0.095
1999	621 872	1345	0.216	626	0.101	878	0.141
2000	604 441	2606	0.431	2244	0.371	2002	0.331
2001	594 634	9888	1.663	1541	0.259	11 376	1.913
2002	596 122	12 371	2.075	91	0.015	7786	1.306
2003†	621 469	3388	0.545	5	0.001	999	0.161
2004†		18		0		0	
Total		30 805		5879		24 084	

*Estimates based on the age distribution from three providers and extrapolated to the nine providers where some data were given.
†Data for the 2003 and 2004 birth cohorts are incomplete, since data collection did not cover the entire period during which these children would have been eligible for vaccination.

What is already known on this topic

- Coverage of combined measles, mumps and rubella vaccines in children in England and Wales is below the levels required to prevent outbreaks of disease.
- The contribution of single antigen vaccines to population protection against each of these three infections has not been previously quantified.

What this study adds

- The estimated numbers of doses of single vaccines used are small in comparison to the number of doses of MMR administered.
- For recent annual birth cohorts these doses of single vaccines could increase routine coverage by around 2% for measles and less for mumps; this would still be below the target levels of population immunity to sustain elimination.
- The providers of single antigen vaccines could not deliver data in the format routinely reported by the NHS and required by WHO for monitoring immunisation programmes.

2% for measles-containing vaccines and less for the other two antigens. Using realistic assumptions, data from the MHRA suggest that a maximum of 5.6% of children born in 2001/2002 may have received single measles and 4.0% mumps vaccines. Rubella vaccine may have been given to more children as it was licensed and available through the NHS during this period, so data were not available on requests for importation from MHRA. To estimate the actual impact of these vaccines on population susceptibility, we would need to know the number of these children who were already immune (mainly through prior MMR vaccine) and the effectiveness of single vaccines when administered in private clinics. Continued efforts to increase vaccine coverage, particularly in the areas with the lowest coverage, such as the recent MMR Capital catch-up campaign,[5] are needed to prevent future outbreaks.

These speculative figures should be treated with caution. For example, the maximum estimate would be lower if children not in the 2001/2002 birth cohorts were vaccinated, which is likely to have occurred. On the other hand, it is possible that children resident in England and Wales may have been vaccinated in other countries. The minimum estimates only extrapolate the data to the 40 clinics from which we have data and not to all 74 clinics that we identified. For measles vaccine, the differences between the minimum and maximum estimates are small, suggesting that we have captured data from the majority of large providers. The proportion of single mumps vaccine notifications that were actually imported was probably much lower than 30% due to lack of availability during the period studied, explaining the larger discrepancy between the figures produced from both sources. It was not possible to distinguish between children receiving their first and second doses of a vaccine or to identify those who may have already received MMR vaccine. We understand that, in the early period, many single vaccine providers were not routinely offering second doses of vaccine but advising blood tests instead. For the later cohorts of children, it is unlikely that they will have received two doses, as most providers advise a gap of 1 year. Therefore, we think that most of the doses reported to us would be a first dose of that antigen for that child.

Although we were able to obtain minimum estimates of coverage for single antigen measles, mumps and rubella vaccines in each birth cohort (table 2), we were unable to determine the number of children who have received one, two or three of the single antigen vaccines. We are thus unable to estimate how many children have been vaccinated against all three infections covered by the MMR vaccine. Although some providers have protocols whereby children should receive all three single vaccines, the results suggest that many children are not protected against all three diseases. Reasons for this may include delay between doses, availability of vaccine (particularly single mumps vaccine) and cost.

The providers of single antigen vaccines could not easily access data that are routinely reported by the NHS and required of governments by the World Health Organization as essential for monitoring immunisation programmes. It was not possible to obtain figures for the number of children who had received two doses by the recommended ages. We also do not know whether the data which were submitted were accurate. We recommend that the Healthcare Commission, which regulates private providers, sets the same standard of data collection and reporting by private clinics as that required of the NHS, consistent with other standards. Options would need to allow reporting from providers to GPs and to local child health systems of all types of vaccine received in both NHS and private healthcare providers, without risk of duplication. Enabling reporting of vaccine coverage, in a format compatible with the COVER programme, should be the standard applied.

On an individual patient level, there is a need for a reliable flow of information on vaccines given and possible adverse events to the child's GP. This would ensure continuity of care and the ability to identify children at risk during an outbreak who may have received a first, but not a second, dose of vaccine. A number of providers expressed an interest in contributing to national vaccine coverage data for these infections and would be willing to develop prospective systems. These figures could then be combined with other routine coverage data to provide better estimates of immunity to measles, mumps and rubella in preschool children.

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